C6 72. The recombinant vector of claim 71, which contains a mutagenized viral genomic sequence that is larger than 200 kb.

IN THE ABSTRACT:

Please amend the abstract to read as follows:

C7 Recombinant vectors containing infectious viral genomic sequences as well as sequences of a cloning vehicle, a cell comprising the vector, a method for producing the vectors, a method of mutagenizing an infectious viral genomic sequence in the vector, and a vector obtained by the method.

REMARKS

The Present Invention

The present invention is directed to a recombinant vector containing an infectious viral genomic sequence larger than 100 kb and a cloning vehicle sequence that is derived from a bacterial artificial chromosome (BAC) and that can be replicated in a host cell, a cell comprising same, a method of producing such a recombinant vector, and a method of mutagenizing an infectious viral genomic sequence in the aforementioned recombinant vector, as well as a vector obtained in accordance with such a method.

Amendment to the Claims and Abstract

Claims 36, 45 and 57 have been amended to point out more particularly and claim more distinctly the present invention. The amendments of claims 36 and 57 are supported by the instant specification in, for example, the paragraph bridging pages 3 and 4, the third full paragraph on page 5, and Example 1. The amendment of claim 45 is supported by the instant specification at, for example, page 4, second full paragraph. Claims 46, 48-50, and 67-70 have been amended to address matters of form. The dependency of claim 72 has been corrected. No new matter has been added by way of these amendments.

The abstract has been amended to delete use of the word "said." No new matter has been added by way of this amendment.

The Pending Claims

Claims 36-72 are currently pending. Claims 36-50 are directed to the recombinant vector, whereas claims 51-56 are directed to the cell comprising same, claims 57-66 are directed to the method of producing such a recombinant vector, claims 67-70 are directed to the method of mutagenizing an infectious viral genomic sequence in the

aforementioned recombinant vector, and claims 71 and 72 are directed to the vector obtained in accordance with such a method.

The Office Action

The Office has set forth the following objection and rejections:

(i) an objection has been raised with respect to the abstract for use of the word "said";

(ii) claims 36-72 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite; and

(iii) claims 36-40, 42, 43, 51 and 52 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Messerle et al.

Reconsideration is hereby requested.

Discussion of Objection to the Abstract

The Office has objected to the abstract for use of the word "said." In view of the amendment of the abstract, this objection is believed to be moot.

Discussion of Rejection under Section 112, second paragraph

Claims 36-72 have been rejected under Section 112, second paragraph, as allegedly indefinite. Specifically, the Office contends that the language "a cloning vehicle sequence...derived from a bacterial artificial chromosome (BAC) and that can be replicated in a host cell..." in claims 36 and 57 is unclear as is the language "wherein said cloning vehicle sequence is flanked by identical sequence sections that enable excision of the cloning vehicle..." in claim 45, that the use of "and/or" in claims 46 and 48-50 is unclear, and that the language "introducing the recombinant vector of claim 36 into a bacterial host cell, which contains DNA molecules..." in claim 67 is unclear. This rejection is believed to be moot in view of the amendments to the claims.

Discussion of Rejection under Section 102(b)

Claims 36-40, 42, 43, 51 and 52 have been rejected under Section 102(b) as allegedly anticipated by Messerle et al. This rejection is traversed for the reasons set forth below.

The BAC/MCMV hybrids of Messerle et al. do not contain infectious viral genomic sequences. See, e.g., the abstract of Messerle et al., wherein it is stated that "[t]ransfection of each plasmid alone into eukaryotic cells did not result in the production of a progeny." Thus, the two individual plasmids described by Messerle et al. do not

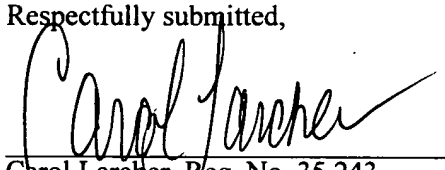
contain infectious viral genomic sequences capable of being replicated and packaged in the viral host. Infectious viral progeny can only be obtained by co-transfection of both plasmids. This is in distinct contrast to the present invention, which provides a single recombinant vector containing an infectious viral genomic sequence larger than 100 kb that can be replicated and packaged in the host cell.

In view of the foregoing, Messerle et al. does not anticipate the rejected claims. Accordingly, Applicants request the withdrawal of this rejection.

Conclusion

In view of the foregoing, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is invited to contact the undersigned attorney.

Respectfully submitted,



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Date: December 20, 2001

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In re Appln. of Koszinowski et al.
Application No. 09/463,890

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APR 2 9 2002
PATENT & TRADEMARK OFFICE
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CERTIFICATE OF MAILING

I hereby certify that this AMENDMENT AND RESPONSE TO OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.

Date: December 20, 2001 Ellen K. Mark

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APR 29 2002
PATENT & TRADEMARK OFFICE

PATENT
Attorney Docket No. 203676

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Koszinowski et al.

Art Unit: 1646

Application No. 09/463,890

Examiner: G. Leffers, Jr.

Filed: January 31, 2000

For: RECOMBINANT VECTOR CONTAINING INFECTIOUS, VIRAL GENOME SEQUENCES GREATER THAN 100 KB, METHOD FOR PRODUCING SAME AND USE FOR THE MUTAGENESIS OF THE VIRAL SEQUENCES

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AMENDMENTS TO CLAIMS AND ABSTRACT
MADE IN RESPONSE TO OFFICE ACTION DATED OCTOBER 2, 2001

Amendments to existing claims:

36. A recombinant vector containing an infectious viral genomic sequence larger than 100 kb and all or a [cloning vehicle sequence that is derived from] portion of a bacterial artificial chromosome (BAC) [and that can be replicated], wherein said all or a portion of the BAC enables replication of the recombinant vector in a host cell.

45. The recombinant vector of claim 36, wherein said [cloning vehicle sequence is flanked by identical sequence sections that enable excision of the cloning vehicle sequence by homologous recombination] all or a portion of the BAC is flanked by nucleotide sequences which are identical to each other and which, upon homologous recombination, enable excision of said all or a portion of the BAC from the recombinant vector.

46. The recombinant vector of claim 36, wherein said [cloning vehicle sequence] all or a portion of the BAC is flanked by (i) recognition sequences for sequence-specific recombinases, (ii) [and/or by] unique restriction enzyme sites, or (iii) recognition sequences for sequence-specific recombinases and unique restriction enzyme sites.

48. The recombinant vector of claim 36, which further contains (i) a selection gene, (ii) [and/or] a marker gene, or (iii) a selection gene and a marker gene.

49. The recombinant vector of claim 45, which further contains (i) a selection gene, (ii) [and/or] a marker gene, or (iii) a selection gene and a marker gene.

50. The recombinant vector of claim 46, which further contains (i) a selection gene, (ii) [and/or] a marker gene, or (iii) a selection gene and a marker gene.

57. A method of producing a recombinant vector of claim 36, which method comprises:

(a) introducing into a host cell containing infectious viral genomic sequences [a cloning vehicle sequence that is derived from a bacterial artificial chromosome (BAC) and that can be replicated in a host cell] all or a portion of a BAC, wherein said all or a portion of the BAC enables replication in the host cell of a recombinant vector of which it is comprised, and

(b) recombining [the cloning vehicle sequence with the infectious viral genomic sequences to obtain the recombinant vector] all or a portion of the BAC, as has been introduced into the host cell, with the infectious viral genomic sequences,

whereupon the recombinant vector is obtained.

67. A method of mutagenizing an infectious viral genomic sequence in a recombinant vector of claim 36, which method comprises:

(a) introducing the recombinant vector of claim 36 into a bacterial host cell, which contains mutagenizing DNA molecules, and

(b) mutagenizing the infectious viral genomic sequence in the recombinant vector.

68. The method of claim 67, wherein step (b) is carried out by homologous recombination between the recombinant vector and the mutagenizing DNA molecules contained in the bacterial host cell.

69. The method of claim 68, wherein there is a mutant allele in the mutagenizing DNA molecules and the homologous recombination is carried out between the recombinant vector and the mutant allele.

70. The method of claim 67, wherein there is a transposon in the mutagenizing DNA molecules and step (b) is carried out by the [using a] transposon.

72. The recombinant vector of claim [71] 67, which contains a mutagenized viral genomic sequence that is larger than 200 kb.

Amendments to the abstract:

[Recombinant vector containing infectious viral genome sequences having a size larger than 100 kb, method for producing same, and use for the mutagenesis of the viral sequences

The present invention relates] Recombinant vectors containing infectious viral [genome] genomic sequences as well as sequences of a cloning vehicle, a cell comprising the vector, [and to] a method for producing [said] the vectors[. Furthermore, the present invention relates to the use of such recombinant vectors, especially for the mutagenesis of the], a method of mutagenizing an infectious viral [genome] genomic sequence[s contained therein, and to a method for the mutagenesis of said sequences] in the vector, and a vector obtained by the method.

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PATENT
Attorney Docket No. 203676

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Koszinowski et al.

Application No. 09/463,890

Filed: January 31, 2000

For: RECOMBINANT VECTOR CONTAINING INFECTIOUS, VIRAL GENOME SEQUENCES GREATER THAN 100 KB, METHOD FOR PRODUCING SAME AND USE FOR THE MUTAGENESIS OF THE VIRAL SEQUENCES

Art Unit: 1646

Examiner: G. Leffers, Jr.

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PENDING CLAIMS AFTER AMENDMENTS MADE IN RESPONSE TO OFFICE ACTION DATED OCTOBER 2, 2001

36. A recombinant vector containing an infectious viral genomic sequence larger than 100 kb and all or a portion of a bacterial artificial chromosome (BAC), wherein said all or a portion of the BAC enables replication of the recombinant vector in a host cell.

37. The recombinant vector of claim 36, wherein the infectious viral genomic sequence is larger than 200 kb.

38. The recombinant vector of claim 36, wherein the infectious viral genomic sequence is derived from a DNA virus.

39. The recombinant vector of claim 38, wherein said DNA virus is a herpes virus.

40. The recombinant vector of claim 39, wherein said herpes virus is a beta herpes virus.

41. The recombinant vector of claim 40, wherein said beta herpes virus is a human cytomegalovirus.

42. The recombinant vector of claim 40, wherein said beta herpes virus is a mouse cytomegalovirus.

43. The recombinant vector of claim 39, wherein said herpes virus is a gamma herpes virus.

44. The recombinant vector of claim 43, wherein said gamma herpes virus is murine gamma herpes virus 68 (MHV 68).

45. The recombinant vector of claim 36, wherein said cloning vehicle sequence is flanked by identical sequence sections that enable excision of the cloning vehicle sequence by homologous recombination.

46. The recombinant vector of claim 36, wherein said cloning vehicle sequence is flanked by recognition sequences for sequence-specific recombinases and/or by unique restriction enzyme sites.

47. The recombinant vector of claim 46, wherein the recognition sequences are loxP sites.

48. The recombinant vector of claim 36, which further contains (i) a selection gene, (ii) a marker gene, or (iii) a selection gene and a marker gene.

49. The recombinant vector of claim 45, which further contains (i) a selection gene, (ii) a marker gene, or (iii) a selection gene and a marker gene.

50. The recombinant vector of claim 46, which further contains (i) a selection gene, (ii) a marker gene, or (iii) a selection gene and a marker gene.

51. A cell containing a recombinant vector of claim 36.

52. A cell containing a recombinant vector of claim 45.

53. A cell containing a recombinant vector of claim 46.

54. A cell containing a recombinant vector of claim 48.

55. A cell containing a recombinant vector of claim 49.

56. A cell containing a recombinant vector of claim 50.

57. A method of producing a recombinant vector of claim 36, which method comprises:

(a) introducing into a host cell containing infectious viral genomic sequences all or a portion of a BAC, wherein said all or a portion of the BAC enables replication in the host cell of a recombinant vector of which it is comprised, and

(b) recombining all or a portion of the BAC, as has been introduced into the host cell, with the infectious viral genomic sequences,

whereupon the recombinant vector is obtained.

58. The method of claim 57, wherein step (b) is carried out by homologous recombination.

59. The method of claim 57, wherein said host cell is a eukaryotic cell.

60. The method of claim 59, wherein said eukaryotic cell is a mammalian cell.

61. The method of claim 60, wherein said mammalian cell is a primary fibroblast, a human foreskin fibroblast (HFF), or a mouse embryonic fibroblast.

62. The method of claim 61, wherein said primary fibroblast is an NIH3T3 fibroblast.

63. The method of claim 57, wherein said cloning vehicle sequence is introduced into the host cell by calcium phosphate precipitation, lipofection or electroporation.

64. The method of claim 57, wherein said cloning vehicle sequence is introduced into the host cell by a viral vector.

65. The method of claim 57, wherein said host cell is a bacterial organism.

66. The method of claim 65, wherein said bacterial organism is *Escherichia coli*.

67. A method of mutagenizing an infectious viral genomic sequence in a recombinant vector of claim 36, which method comprises:

(a) introducing the recombinant vector of claim 36 into a bacterial host cell, which contains mutagenizing DNA molecules, and

(b) mutagenizing the infectious viral genomic sequence in the recombinant vector.

68. The method of claim 67, wherein step (b) is carried out by homologous recombination between the recombinant vector and the mutagenizing DNA molecules.

69. The method of claim 68, wherein there is a mutant allele in the mutagenizing DNA molecules and the homologous recombination is carried out between the recombinant vector and the mutant allele.

70. The method of claim 67, wherein there is a transposon in the mutagenizing DNA molecules and step (b) is carried out by the transposon.

71. A recombinant vector obtained in accordance with the method of claim 67.

72. The recombinant vector of claim 71, which contains a mutagenized viral genomic sequence that is larger than 200 kb.

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1646 **PATENT**
Attorney Docket No. 203676
Date: December 20, 2001

In re Application of: Koszinowski et al.
Application No. 09/463,890
Filed: January 31, 2000
For: RECOMBINANT VECTOR CONTAINING INFECTIOUS, VIRAL GENOME SEQUENCES GREATER THAN 100kb, METHOD FOR PRODUCING SAME AND USE FOR THE MUTAGENESIS OF THE VIRAL SEQUENCES

COMMISSIONER FOR PATENTS
Washington, D.C. 20231

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Sir:

Transmitted herewith is an Amendment and Response to Office Action.

☐ Applicants claim small entity status of this application under 37 CFR 1.27.

☒ Petition for Extension of Time
- ☐ Applicants petition for a one-month extension of time under 37 CFR 1.136, the fee for which is $110.00 (enclosed).
- ☒ Applicants believe that no petition for an extension of time is necessary. However, to the extent that such petition is deemed necessary, Applicants hereby petition for a sufficient extension of time to render the present submission timely. Please charge Deposit Account No. 12-1216 for the appropriate petition fee.

☒ No additional claim fee is required.

☒ Other: Amendments to Claims and Abstract Made in Response to Office Action Dated October 2, 2001, Pending Claims After Amendments Made in Response to Office Action Dated October 2, 2001

The claim fee has been calculated as shown below:

					Small Entity		Other Than A Small Entity	
	Claims Remaining After Amendment		Highest Number Previously Paid For	Extra Claims Present	Rate	Addit. Claim Fee	Rate	Addit. Claim Fee
Total	37	Minus	37	=0	x 9=	$	x 18=	$0
Independent	1	Minus	2	=0	x 42=	$	x 84=	$0
☐ First Presentation of Multiple Claim					+ 140=	$	+ 280=	$0
					Total	$	Total	$0

☐ Please charge my Deposit Account No. 12-1216 in the amount of $. A duplicate copy of this sheet is attached.

☐ A check in the amount of $ is attached.

☒ The Commissioner is hereby authorized to charge any deficiencies in the following fees associated with this communication or credit any overpayment to Deposit Account No. 12-1216. A duplicate copy of this sheet is attached.
- ☒ Any filing fees under 37 CFR 1.16 for the presentation of extra claims.
- ☒ Any patent application processing fees under 37 CFR 1.17.

Respectfully submitted,

LEYDIG, VOIT & MAYER, LTD.

By _____
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